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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,337	BENOIT ET AL.	
	Examin r	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *34-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33,38 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office Action is a response to the Election filed October 20, 2003.

Claims 1-39 are pending in the instant application.

Claims 34-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement on October 20, 2003.

Claims 1-33, 38 and 39 have been on the merits.

Election/Restrictions

Applicant's advised the Examiner that the listing of claims corresponding to the alleged invention appears to be incorrect. Applicants contend that claims 1-2, 6, 8, 10, 12, 13, 16, 18, 20, 22, 24, 26, 28, 30 and 32 recite a polynucleotide comprising a fragment of SEQ ID NO:1 and claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 39 recite a polynucleotide comprising a fragment of SEQ ID NO:2. The Examiner appreciates the Applicants careful review of the claims and agrees that the listing of claims is incorrect. Therefore, Group I consists of claims 1-2, 6, 8, 10, 12, 13, 16, 18, 20, 22, 24, 26, 28, 30 and 32 reciting a polynucleotide comprising a fragment of SEQ ID NO:1 and Group II consists of claims 4, 5, 7, 9, 11, 14, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, and 39 reciting a polynucleotide comprising a fragment of SEQ ID NO:2. It is noted that the claims recited in Groups III, IV, V, and VI remain unchanged.

Applicant's election with traverse of Group I (1-2, 6, 8, 10, 12, 13, 16, 18, 20, 22, 24, 26, 28, 30 and 32), filed October 20, 2003 is acknowledged. The traversal is two-fold. The first

traversal is on the ground(s) that the restriction between Groups I and II is improper because the restriction between Groups I and II encompass homologs derived from different species. This traversal is found persuasive and Groups I and II will be examined together since Group I recites claims drawn to a polynucleotide comprising SEQ ID NO:1 (the polynucleotide sequence upstream of the gene encoding the mouse CARP protein) and Group II recites claims drawn to a polynucleotide comprising SEQ ID NO:2 (the polynucleotide sequence upstream of the gene encoding the human CARP protein). The second traversal is on the ground(s) that the requirement for restriction between Groups III-VI appears to be based on the recitation of SEQ ID NO:1 and SEQ ID NO:2 and is therefore improper. This traversal is not found persuasive because while Groups III-VI are based on the recitation of SEQ ID NO:1 and SEQ ID NO:2, the inventions of Groups III-VI are distinct and independent from the inventions of Groups I and II, as detailed in the previous Restriction Requirement, filed September 23, 2003. However, it is noted that if Applicant, instead of Group I, elected Group III, the Examiner would have examined Groups III and IV together in light of Applicants first traversal. Similarly, if Applicant, instead of Group I, elected Group V, the Examiner would have examined Groups V and VI together.

In light of Applicants traversal, Groups I and II (claims 1-33, 38 and 39) will be examined on the merits.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The Information Disclosure Statement, filed October 30, 2003 is acknowledged. The references referred to therein have been considered by the Examiner.

Priority

The reference to priority to Application USSN 60/251,582, filed December 7, 2000 in the first sentence of the Specification is acknowledged.

Specification

The abstract of the disclosure is objected to because it comprises three paragraphs. An abstract should contain only a single paragraph. See MPEP § 608.01(b). Correction is required.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because:
> The fourth inventor has made non-initialed and/or non-dated alterations to the oath or declaration. See 37 CFR 1.52(c).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 2, and 4 are rejected under 35 U.S.C. 102(a) as being anticipated by Aihara et al. [GenBank Accession Number AF131884, Database DDBJ, submitted February 15, 2000].

Claims 1, 2, and 4 are drawn to polynucleotide fragments of SEQ ID NO:1 or SEQ ID NO:2.

It is noted that the limitations "a polynucleotide comprising a fragment of SEQ ID NO:1" and "a polynucleotide comprising a fragment of SEQ ID NO:2" of claims 1 and 4, respectively are given their broadest reasonable interpretations since the term "fragment" is not defined by the claims and the specification does not provide a standard for ascertaining the requisite degree of the term "fragment". Therefore, the limitations "a polynucleotide comprising a fragment of SEQ ID NO:1" and "a polynucleotide comprising a fragment of SEQ ID NO:2" have been broadly

interpreted as any polynucleotide comprising at least a 2 bp fragment of SEQ ID NO:1 or any polynucleotide comprising at least a 2 bp fragment of SEQ ID NO:2.

Aihara et al. disclose a 2074 bp sequence fragment of the human CVARP 5'-flanking region.

Therefore Aihara et al. anticipate claims 1, 2, and 4.

Claims 1-7, 20-27, 30, 31, 32, 33, 38, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuo et al. (Development, 1999 Vol. 126:4223-4234).

Claims 1-7, 20-27, 30, 31, 32, 33 are drawn to polynucleotide fragments of SEQ ID NO:1 or SEQ ID NO:2, an expression cassette comprising a sequence encoding a protein or an RNA linked to said polynucleotide fragments, and a vector comprising said expression cassette. Claims 38 and 39 are drawn to polynucleotide fragments of SEQ ID NO:1 or SEQ ID NO:2 and a vector comprising said polynucleotide fragments, which is any DNA not encapsulated by viral proteins.

Please note the broad interpretation of the limitations "a polynucleotide comprising a fragment of SEQ ID NO:1" and "a polynucleotide comprising a fragment of SEQ ID NO:2" of claims 1 and 4, respectively on page 6 above.

Kuo et al. disclose the cloning of a 10 Kb fragment of the mouse CARP gene and the sequencing of a 2.5 Kb fragment upstream of the coding sequence. Kuo et al. further disclose the identification of 5' *cis* regulatory elements that control the cardiac specificity of the CARP gene by the design of luciferase reporter constructs whose expression were driven by 5' nested deletions of the mouse CARP promoter in the pXP2 plasmid (see Figure 3A). Kuo et al. further

disclose deletions from the 5'-end of the fragment were made and showed that a region of 213 bp of the promoter between nucleotides –166 and +47, relative to the transcription start position +1, was sufficient to confer cardiospecific expression *in vitro*, which suggested the presence, at the 5'-end, of an element for controlling the specificity of the promoter (see Figure 3C). Kuo et al. also generated transgenic mouse lines comprising a fragment of 2.5 Kb upstream of the CARP gene, showing specific expression of a transgene in cardiac and skeletal muscle cells at an early stage of embryonic development, this expression then being inhibited during development (see Figure 6).

Therefore, Kuo et al. anticipate claims 11-7, 20-27, 30, 31, 32, 33, 38, and 39.

Claims 1-7, 20-25, 28, 29, 30, 31, 32, and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by Chien et al. [WO 00/15821].

Claims 1-7, 20-25, 28, 29, 30, 31, 32, and 33 are drawn to polynucleotide fragments of SEQ ID NO:1 or SEQ ID NO:2, an expression cassette comprising a sequence encoding a protein or an RNA linked to said polynucleotide fragments, and a vector comprising said expression cassette.

Please note the broad interpretation of the limitations "a polynucleotide comprising a fragment of SEQ ID NO:1" and "a polynucleotide comprising a fragment of SEQ ID NO:2" of claims 1 and 4, respectively on page 6 above.

Chien et al. disclose a portion 5' of the coding sequence of the mouse CARP gene, situated between nucleotides –2285 and +62, relative to the transcription start position +1. This sequence was evaluated in particular for its *in vivo* activity in adenoviral vectors (see Abstract

and SEQ ID NOs. 1 and 2). The levels of activity obtained remain very low, however, such that it was found to be necessary, in order to detect an activity *in vivo*, to isolate the promoter sequence between two inverted terminal repeats of an adeno-associated virus (AAV-ITR) (see Figures 1 and Example 2).

Therefore, Chien et al. anticipate claims 1-7, 20-25, 28, 29, 30, 31, 32, and 33.

Claims 1-5, 8, 9, and 12-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Phillip et al. (Clinical Cancer Research, 1996 Vol. 2:59-68).

Claims 1-5, 8, 9, and 12-15 are drawn to polynucleotide fragments of SEQ ID NO:1 or SEQ ID NO:2, an expression cassette comprising a sequence encoding a protein or an RNA linked to said polynucleotide fragments, and a vector comprising said expression cassette, wherein the protein or RNA of therapeutic interest is a vascular endothelial growth factor, a fibroblast growth factor, an angiopoietin, or a cytokine.

Please note the broad interpretation of the limitations "a polynucleotide comprising a fragment of SEQ ID NO:1" and "a polynucleotide comprising a fragment of SEQ ID NO:2" of claims 1 and 4, respectively on page 6 above.

Phillip et al. disclose gene modification of primary tumor cells for active immunotherapy of human breast and ovarian cancer. Phillip et al. further disclose the design of two plasmid constructs pMP1IL2 and pMP6IL2, expressing IL-2 (see Figure 1). Phillip et al. further disclose the transfection of pMP1IL2 and pMP6IL2 in MCF7 breast cancer cells increased IL-2 gene expression (see Figures 3 and 4).

Therefore, Phillip et al. anticipate claims 1-5, 8, 9, and 12-15.

Claims 1-5, 10, 11, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Alarco et al. (Journal of Bacteriology, 1999 Vol. 181:700-708).

Claims 1, 3, 4, 5, 10, 11, and 12 are drawn to polynucleotide fragments of SEQ ID NO:1 or SEQ ID NO:2, an expression cassette comprising a sequence encoding a protein or an RNA linked to said polynucleotide fragments, and a vector comprising said expression cassette, wherein the protein or RNA of interest is an activating or inhibiting transcription factor.

Please note the broad interpretation of the limitations "a polynucleotide comprising a fragment of SEQ ID NO:1" and "a polynucleotide comprising a fragment of SEQ ID NO:2" of claims 1 and 4, respectively on page 6 above.

Alarco et al. disclose the bZip transcription factor Cap1p is involved in multidrug resistance and oxidative stress response in *Candida albicans*. Alarco et al. further disclose the expression of Cap1p in CJD21 cells transformed with plasmid pMK22 carrying the full-length Cap1 gene or a hyperactive allele of Cap1 (see Figure 2).

Therefore, Alarco et al. anticipate claims 1-5, 11, and 12.

Claims 1-5, 16, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Mohuczy et al. (Hypertension, 1999 Vol. 33:354-359).

Claims 1, 3, 4, 5, 16, and 17 are drawn to polynucleotide fragments of SEQ ID NO:1 or SEQ ID NO:2, an expression cassette comprising a sequence encoding a protein or an RNA linked to said polynucleotide fragments, and a vector comprising said expression cassette, wherein the protein or RNA of interest is an antisense RNA or ribozyme.

Please note the broad interpretation of the limitations "a polynucleotide comprising a fragment of SEQ ID NO:1" and "a polynucleotide comprising a fragment of SEQ ID NO:2" of claims 1 and 4, respectivcly on page 6 above.

Mohuczy et al. disclose the antisense inhibition of AT_1 receptor in vascular smooth muscle cells using adeno-associated virus (AAC) based vector. Mohuczy et al. further disclose the inhibition of AT_1 receptor expression in vascular smooth muscle cells following transfection of an AAC vector containing AT_1 receptor cDNA in the antisense orientation.

Therefore, Mohuczy et al. anticipate claims 1-5, 16, and 17.

Claims 1-5, 18, and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (Circulation Research, 1998 Vol. 82:862-870).

Claims 1-5, 18, and 19 are drawn to polynucleotide fragments of SEQ ID NO:1 or SEQ ID NO:2, an expression cassette comprising a sequence encoding a protein or an RNA linked to said polynucleotide fragments, and a vector comprising said expression cassette, wherein the protein of therapeutic interest is nitric oxide synthetase, superoxide dismutase, or catalase.

Please note the broad interpretation of the limitations "a polynucleotide comprising a fragment of SEQ ID NO:1" and "a polynucleotide comprising a fragment of SEQ ID NO:2" of claims 1 and 4, respectively on page 6 above.

Chen et al. disclose the overexpression of human endothelial nitric oxide synthase in rat vascular smooth muscle cells and in balloon-injured carotid artery (see Abstract). Chen et al. further disclose the design of a human endothelial nitric oxide synthase viral vector by inserting

human endothelial nitric oxide synthase into the *Eco*RI site of the parental retroviral vector LXSN (see page 863, first column).

Therefore Chen et al. anticipate claims 1-5, 18 and 19.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (703) 306-3221. The examiner can normally be reached on M-F 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 746-8693.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

tcg
November 20, 2003

KAREN A. LACOURCIERE, PH.D
PRIMARY EXAMINER